INFECTIOUS FEVERS - CLINICAL PROFILE OF 500 CASES

Dissertation submitted to

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERSITY

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M.D. BRANCH - I

GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL

THE TAMIL NADU Dr.M.G.R.MEDICAL UNIVERSITY

CHENNAI, INDIA

MARCH - 2008

CERTIFICATE

This is to certify that the dissertation titled "**INFECTIOUS FEVERS - CLINICAL PROFILE OF 500 CASES"** is the bonafide original work of **Dr.S.MURUGANANTH,** in partial fulfillment of the requirements for M.D., Branch - I, (General Medicine) Examination of the Tamil Nadu Dr.M.G.R. Medical University to be held in March 2008. The period of study was from May 2006 to May 2007.

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I am also thankful to my colleagues for their full cooperation in this study and my sincere thanks to all the patients who co-operated for this study.

DECLARATION

I, **Dr.S.MURUGANANTH**, solemnly declare that this dissertation "**INFECTIOUS FEVERS - CLINICAL PROFILE OF 500 CASES"** is a bonafide record of work done by me in the Department of Medicine, Government Stanley Medical College and Hospital, Chennai under the guidance of **Prof.Dr.S.SHIVAKUMAR, M.D.,** Professor of Therapeutics, Government Stanley Medical College and Hospital, Chennai – 600 001.

This dissertation is submitted to the Tamilnadu Dr.M.G.R.Medical University, Chennai in partial fulfillment of the University regulations for the award of MD Degree (General Medicine) Branch-I, Examination to be held in March 2008.

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Sub: Medical Education – Stanley Medical College, Chennai – Ethical Committee constituted for approval of Dissertation/ Thesis submitted – regarding.

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The Ethical Committee meeting was held on 3-9-2007 and 7-9-2007 to discuss the paper submitted for Dissertation /Thesis.

The following Members of the Ethical Committee were present and discuss in detail for the approval of the papers presented by the individual by means of power point presentation.

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Dr.Thenmozhivalli, Prof. of Microbiology,
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ETHICAL MEETING

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1."N.O.C. for PMS study of pregabalin" - Dr.Parimalam Kumar
2. " A Phase IIb/III trial of LLL-3348 of lupin ltd in plaque psoriasis - Dr.A.Ramesh

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(2)Psychological autopsy of suicide.

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4.Dr. K. Babu - M3 - P.G.

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9.Dr.N.Jayanthi. M6- PG

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11.Dr.R.Geetha - Pharmacology

Evaluation of the sedative effects produced by antihistamines inhealthy volunteers by new techniques.

12.Dr.K.G.Devibala, Pharmacology

To evaluate the efficacy of rupatadine in controlling pruritis in lichen planus.

13.Dr.B.Anitha, Physiology

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14.Dr.M.Thirumaran, Physiology

Heart rate variability analysis in alcohol dependant individuals.

15.Dr.K.Vinod, Anaesthesia

Real time ultra sound guided catheterization of IJV – A prospective comparison with land mark guided technique.

16.Dr.Rajesh. C.P. – M6 – PG

Cardiac conduction abnormalities and asymptomatic myocardial infarction in NIDDM patients.

The papers presented to the Committee members by the Profs./Asst. Prof./Post Graduates/Under graduates were discussed across the table while their presentation.

The above papers discussed in detail with its supportive documents submitted by them and approved the above papers submitted for Ethical Committee.

Name of the Members	Signature
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CONTENTS

INTRODUCTION

Infections are one of the leading cause of morbidity and mortality in our country. The changing profile of infections need to be determined in order to focus on specific investigative and therapeutic measures. This study was undertaken to evaluate the changing profile in patients presenting with infectious fevers.

AIM OF THE STUDY

To study the clinical and laboratory profile of patients with infectious fever in the medical wards of Government Stanley Medical College and Hospital.

The groups analysed were :

1. Fever of less than 5 days with
    a. Organ dysfunction
    b. Temperature >40°C
2. Fever of more than 5 days with or without organ dysfunction.

OBJECTIVES

1. To study the clinical profile like age, sex, fever duration and associated systemic symptoms in patients with infectious fever.

2. To study the most common cause of infectious fever.

3. The study the various organ dysfunction and the causes for organ dysfunction in patients with infectious fever.

4. To analyse the causes of mortality in patients with infectious fever.

5. To compare and analyse with the etiological profile of the previous study done at our hospital in 2002 - 2003.

REVIEW OF LITERATURE

FEVER[1]

Definition

Fever is an elevation of the body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in hypothalamic set point, which controls the normal body temperature.

Mechanism

Once the hypothalamic set point is raised, neurons in the vasomotor centre is activated and vasoconstriction commences, shunting of blood away from the periphery decreasing heat loss. This mechanism increases the body temperature by 1° to 2°C. Shivering begins at this point of time which further increases the body temperature. Heat production by liver also increases.

Control of body temperature

Body temperature is controlled by hypothalamus. Neurous in both pre optic anterior hypothalamus and the posterior hypothalamus receives two kinds of signals; one from the peripheral nerves that reflect warmth and cold receptors and other from the temperature of blood bathing the region, which are integerated to maintain the normal body temperature. A normal body temperature is ordinarily maintained despite environmental variations, because of the balance between heat production and heat dissipation.

Normal Temperature

According to studies, the mean oral temperature is 36.8° ± 4°C (98.2 ± 0.7°F) with low levels at 6 am and higher levels at 4 to 6 pm. In light of these studies an AM temperature of >37.2°C (98.9°F) or a PM temperature > 37.7°C (99.9°F) would define fever. Rectal temperatures are generally 0.4°C higher than oral readings. Lower oesophageal temperatures closely reflect core temperature.

A fever of >41.5°C (>106.7°F) is called hyperpyrexia.

Fever Patterns

Intermittent fevers are temperature elevations that return to normal at least once during most days.

Continous fevers do not vary more than 1°F. Remittent fevers do not return to normal each day. Relapsing fevers are recurrent over days or weeks and may have any undergoing fever pattern.

Studies of FUO (Fever of Unknown Origin)

Kejariwal et al.,[2] in 2001 at Calcutta studied the etiological profile of 100 cases of FUO, the pattern was infections (53%) followed by neoplasm (17%), collagen vascular diseases (11%), miscellaneous (5%) and undiagonosed (14%).

De Kleijn et al.,[3] in a study of 167 immunocompetent patients with FUO found 43 (25.7%) had infections, 21 (12.6%) had neoplasms and 40 (24.0%) had inflammatory diseases.

Petersdorf et al.,[4] in 1952 - 57, studied 100 cases, of which majority (36%) were due to infections like, tuberculosis, abdominal abscess, endocarditis, brucellosis and urinary tract infections. 26% were due to lymphomas, leukemias and solid tumors. 15% were due to connective tissue diseases.

Larson et al., [5] studied 105 cases of FUO patients of which infections formed 30%. Malignancies formed 37% and 14.3% were due to connective tissue disorders. Others were undiagnosed.

Knockaert et al., [6] studied 199 cases of FUO patients of which infections formed 22.5%, followed by collagen vascular disorders (21.5%). Neoplasms formed 7% while others were miscellaneous and undiagnosed.

Sharma et al., [7] studied 150 cases of FUO of which, infections formed 50%, followed by Neoplasms which formed 22%. 8% were due to collagen vascular diseases, 15% formed miscellaneous causes and 5% were undiagnosed.

Burke et al., [8] reviewed various studies on FUO and noted that common treatable causes were tuberculosis, subacute bacterial endocarditis, abscesses, salmonella and leptospirosis.

STUDIES ON ETIOLOGY OF FEVER

Shivakumar et al.,[9] reported the study on etiology profile of fever, a study carried out in Chennai during 2002 - 2003. Out of 195 diagnosed cases tuberculosis formed 40% of cases, pneumonia 15.4%, meningitis and malaria forming 12.8% each and leptospirosis forming 8.2%. The proportion of undiagnosed cases was 46%.

Ruth D. Ellis et al.,[10] studied to find out the etiological profile of fever in the Thailand, which was carried out from 1999 to 2002. Etiologic diagnosis was made in 48% cases. Malaria was the most common diagnosis accounting for 25%, followed by leptospirosis, comprising about 17%. Other etiologic diagnosis were intestinal infections, dengue fever and typhoid.

LITERATURE ON INDIVIDUAL FEVERS

MALARIA

PROBLEM STATEMENT

WORLD[11]

- 107 countries has areas of risk of malaria transmission.
- 3.2 billion people live in areas of risk of malaria transmission.
- 350 - 500 million malaria episodes occur annually.
- 1 million malaria deaths occur annually.

INDIA[12]

In 2006, there were 1.04 million vivax malaria cases and 0.46 million falciparum cases reported in India. There were 890 deaths due to malaria.

MALARIAL SPECIES

There are four species of human malarial parasite i.e. Pl.vivax, Pl.falciparum, Pl.malariae and P1.ovale. In India 60 - 65% of infections are due to Pl.vivax and 35 to 45% are due to Plasmodium falciparum.

Antigenic diversity is present among different malarial parasites and also within the species.

SEVERE MALARIA

Severe malaria is usually caused by Pl.falciparum but recently it has been reported in Pl.vivax cases in Indian Subcontinent.

CLINICAL FEATURES

Uncomplicated malaria :

The clinical features of complicated malaria are common to all species. Head ache, muscular ache, abdominal discomfort, lethargy and lassitude often precede fever by about 2 days.

The fever in Plasmodium vivax and Plasmodium ovale regularises to a two day cycle and in Plasmodium malaria to a 3 day cycle. The fever in Pl.falciparum may never regularise to a classical tertian pattern.

DEFINITION OF SEVERE MALARIA BY WHO[13]

1. Renal failure : Sr.creatinine > 3 mgs / dl
   Urine output < 400 ml / 24 hrs (or)
   < 12 ml / hr
2. Severe Anaemia Hb% < 5 gms % (or)
   Hct < 15%
3. Cerebral malaria : Unarousable coma with peripheral parasitemia
4. Pulmonary Oedema or acute respiratory distress syndrome
5. Hypoglycemia : Blood sugar < 40 mg / dl
6. Shock - Systolic BP < 70 mm Hg (Adults)
   < 50 mm Hg (Children - 1-5 yrs)
7. Acidemia - pH < 7.33, Hco3 < 15 mq / l
8. Spontaneous bleeding : Gums, Nose and GIT due to DIC
9. Macroscopic haemoglobinuria
10. Seizures > 3 episodes
11. Hyperparasitemia - More than 20%
12. Jaundice : Serum bilirubin > 3 mgs / dl is a marker of severe malaria, only when combined with other vital organ dysfunction (i.e. cerebral malaria and renal failure).

The 2000 WHO recommendation also include the following under severe malaria.

1. Impairment of consciousness less marked than unarousable coma.

2. Prostration - Inability to sit unassisted in a child who is normally able to do so. In a child not old enough to sit this is defined as inability to feed.

STUDIES OF MALARIA

Bansode et al,[14] conducted a prospective study of malaria at Bombay during June 1993 to May 1994. All patients had fever, followed by head ache (92%), vomitting (74%), cough (7%), diarrhoea (4.6%), icterus (3.8%) and oliguria (1%) 70% were due to Plasmodium vivax and 30% due to Pl.falciparum.

Madhu Muddaiah et al.,[15] in mangalore in 2002 - 2004 studied the profile of 190 admitted patients with smear positive malaria. Plasmodium vivax - 90, Plasmodium falciparum-71, mixed infections - 29. Jaundice occurred in 5 cases of vivax, 20 cases of falciparum and 3 cases of mixed infections. Over all 28 (14.73%) had jaundice. Splenomegaly was seen in 30 (15.7%), hepatosplenomegaly in 26 (13.6%), hepatomegaly in 8 (4.2%) and raised serum creatinine in 14 (11.57%) cases.

Mohapatra et al.,[16] from Berhampur has reported various atypical presentation of malaria in their study of 110 cases of vivax malaria. They were absence of malarial paroxysm (22.8%), migrainous head ache (4.5%), myalgia (6.3%), episodic utricarial rash (1.8%), relative bradycardia (13.6%) and postural hypotension (2.7%).

Chowta et al.,[17] in 2003 studied 54 patients of both Plasmodium vivax and Plasmodium falciparum and noted chloroquine resistance in 9(16%) patients.

CHANGING TRENDS IN INDIA

The spectrum of severe falciparum malaria has changed world wide. Currently a large proportion of cerebral malaria patients present with multiple complications including acute renal failure and jaundice[18].

Mohapatra et al.,[16] in 2006 from Orissa observed that jaundice is an important solitary complication. There were multiple complications and majority had constellation of 3 complications. Cerebral malaria, jaundice and renal failure (75.3%) were the most common combination. The mortality rate was 14.6%, 21.3%, 30.9%, 38.5%, 100% and 100%, among patients with 1, 2, 3, 4, 5 and 6 combinations respectively.

SEVERE VIVAX MALARIA

Pl.vivax is usually presumed to cause only uncomplicated malaria but in the last few years there has been many reports regarding severe vivax malaria. In a recent study from **Bikaneer, Kochar et al.,**[19] reported 11 cases of definite severe vivax malaria. In all these cases Plasmodium falciparum infection was ruled out by PCR (polymerase chain reaction). All other infectious causes were ruled out by appropriate tests. In this study the manifestations observed were jaundice and hepatic dysfunction in four, severe anaemia in four, cerebral malaria in three, ARDS in three, bleeding diathesis in one and MODS (multi organ dysfunction syndrome) in five patients. Recently in a monograph on

treatment of malaria by WHO in 2006 the terminology of severe vivax malaria has been accepted seperately and it had advocated the same regimen of treatment as for severe falciparum malaria.

LEPTOSPIROSIS[20]

Epidemiology

It is caused by leptospira interrogans complex which has over 20 serogroups and more than 200 serovars. Rodents, domestic and wild animals form the reservoir of infection, whereas domestic animals such as cattle, dogs, pigs may act as carriers for several months (temporary carrier) and rodents usually remain carrier through out life (permanent carrier).

1. Anicteric Leptospirosis

Presents with fever, head ache, body pain and biphasic illness. It has abrupt onset with chills, rigor, fever, head ache and body pain. The most characteristic finding on examination is severe myalgia and conjunctival suffusion. A transient rash can occur. The septicemic phase subsides after 7 - 14 days. The second phase (immune phase) is characterized by severe head ache and low grade fever lasting 4 - 30 days.

2. Icteric Leptospirosis

In some patients, the septicemic phase instead of subsiding progresses to a severe icteric illness with renal failure. Some of the important clinical features are as follows;

Kidneys : Renal involvement is the most serious complication and is the commonest cause of death. Renal manifestations range from urinary sediment changes (pyuria, haematuria and granular casts) to severe renal failure. Renal manifestations are observed commonly in all forms of leptospirosis regardless of the severity of disease or of the infecting sero - group.

Liver : Jaundice is the most important clinical feature of severe illness. Jaundice occurs between the fourth to sixth day but may occur as early as the second day or as late as ninth day, deepens rapidly, reaching a peak within a week. The liver is often enlarged and tender. Jaundice is mainly due to hepatocellular damage. However, hepatocellular necrosis is usually mild and additional factors include intrahepatic cholestasis and increased bilirubin load from absorption of tissue haemorrhage. Marked elevation of serum bilirubin with mildly elevated transaminases is characteristic. Death is rarely due to hepatic failure.

DIAGNOSIS

Modified Faine's criteria is widely used to diagnose leptospirosis.

Faine's Criteria Part A : Clinical Data		**Modified Faine's Criteria Part A : Clinical Data**	
Question	**Score**	**Question**	**Score**
Headache	2	Headache	2
Fever	2	Fever	2
Temp > 39°C	2	Temp > 39°C	2
Conjunctival suffusion	4	Conjunctival suffusion	4
Meningism	4	Meningism	4
Muscle pain	4	Muscle pain	4
Conjunctival suffusion Meningism Muscle pain	10	Conjunctival suffusion Meningism Muscle pain	10
Jaundice	1	Jaundice	1
Albuminuria / Nitrogen Retention	2	Albuminuria / Nitrogen Retention	2
Total score		Total score	
Part B : Epidemiological factors		**Part B : Epidemiological factors**	
Contact with animals or contact with known contaminated water	10	Rainfall Contact with contaminated environment Animal contact Total	5 4 1 10
Part C : Bacteriological and Lab Findings		**Part C : Bacteriological and Lab Findings**	
Isolation of leptospira in culture-Diagnosis certain		Isolation of leptospira in culture - Diagnosis certain	
Positive Serology (MAT) Leptospirosis Endemic		Positive Serology	
Single positive-Low titre Single positive-High titre **Leptospirosis Non Endemic** Single positive-Low titre Single positive-High titre Rising titre (Paired sera) Total (A+B+C)	2 10 5 15 25	ELISA IgM positive SAT - Positive MAT - Single high titre Rising titre (Paired sera) Total (A+B+C)	15 15 15 25

Total score of more than 25 is considered to represent leptospiral disease in modified Faine's criteria.

TREATMENT

Anicteric and milder forms of disease are treated with Doxycycline while severe disease is treated with crystalline penicillin.

STUDIES ON LEPTOSPIROSIS

M.A.Muthusethupathi, S.Shivakumar[21] studied the epidemiological and clinical profile of leptospirosis patients admitted in Government General Hospital, Chennai - 3, (1987 - 1995). Out of 206 patients most of them presented during the monsoon months. The important clinical features noted were :

a. Fever - 100%

b. Jaundice - 83%

c. Renal failure - 79%

d. Myalgia - 79%

e. Conjunctival Suffusion - 43%

f. CNS - 43%

g. Bleeding tendencies - 28%

Autumnalis was the most common serogroup noted then.

Overall icteric leptospirosis constituted the common group with 83% and mortality was 15.5%.

Sumathi G. et al.,[22] reported the serodiagnosis results of leptospirosis from 1995 - 1997, during which microscopic agglutination test revealed that the predominant serovar to be autumnalis (48.3%) and ictero haemorrhagiae (31.1%).

In **2006, Shivakumar S**[23] reported that severe leptospirosis has declined, mild leptospirosis has increased. He reports that in a recent study of 106 cases of leptospirosis from North Chennai, jaundice occurred in 17.8% and renal failure occurred in 10.3% showing a decline in complication. Fever, head ache and myalgia were the common presentation. Only 2 patients were dialysed and there were no deaths. Contaminated environment (98%) and rainfall (50%) were the important epidemiological risk factors.

Muthusethupathi et al.,[24] studied the clinical and serological profile in 57 patients. All had fever followed by jaundice (84%), mylagia (82%), acute renal failure (72%) and conjunctival suffusion (58%). 23 cases underwent dialysis. Autumnalis was the serogroup most commonly recorded.

Lecour et al.,[25] studied 50 cases of leptospirosis and reported renal failure in 62%, aseptic meningitis in 24% with leptospira ictero haemorrhagiae responsible for 78% of cases.

TUBERCULOSIS

PROBLEM STATEMENT[26]

WORLD

9 million cases occur world wide annually

54 million people are infected annually

2.4 million deaths occur annually

INDIA

- 20% of the total cases in the world.
- 1.8 million cases occur annually
- 30,000 patients become smear positive every year.
- Death rate is 100 - 200 / lakh / year.
- It is mostly prevalent in the productive age group of 25 - 45 yrs.

Even though TB is a major global health problem, there are only a few studies about the pattern and profile of its presentation.

Samal et al.,[27] analysed clinical features and evaluated changing trends in 110 non - drug resistant sputum positive pulmonary tuberuclosis between 1987 - 1989. Majority had haemoptysis (60.7%), cough (47.06%) and fever (44.7%). Other symptoms were hoarseness of voice and loss of weight. 18% had clubbing and 3.5% had lymphadenopathy. Radiologically 98% had fibro caseous lesions, cavity in 60% and bilateral opacities in 59%.

Dehankar et al.,[28] studied X-ray changes in pulmonary tuberculosis. 27% had bilateral lesions, 27% had right lower lobe apical segment lesion, and 14% in basal segment. Lingula and whole left lower lobe was less commonly involved. 41% was AFB positive on smear examination.

PNEUMONIA

Community acquired pneumonia continues to be a common and serious disease in both developed and developing countries.

Bansal .S et al.,[29] studied the clinical and bacteriological profile of community acquired pneumonia in a tertiary care hospital at Himachal Pradesh. 70 patients were studied. Patients older than 40 years were predisposed. Etiological diagnosis was obtained in 53(75%) cases. Among that 19 cases of Streptococcus pneumoniae, 12 cases of Klebsiella pneumoniae, 9 cases of Staphylococcus aureus, 8 cases of Mycoplasma pneumonia and 6 cases of Escherichia coli were grown in culture.

CO-INFECTION OF MALARIA AND LEPTOSPIROSIS

In many parts of the world where both malaria and leptospirosis are endemic co-infection with both malaria and leptospirosis is common. Ruth D Ellis in a study in Bangkok from 1999 to 2003, reported 5.12% of coinfection of malaria and serologically proven leptospirosis in a total of 613 cases[10].

ENTERIC FEVER

Chowta MN et al.,[30] in mangalore studied the clinical profile and antibiotic response in typhoid fever from 1999 - 2001. In his study of 44 cases he noted ciprofloxacin resistance in 18.1% of cases. Yew et al.,[31] in his study of clinical profile of enteric fever reported splenomegaly in 47%.

BACTERIAL MENINGITIS

Pomeroy et al.,[32] studied the clinical profile of meningitis and reported seizures in 30% of cases.

CONTRIBUTIONS OF INFECTIONS IN INDIAN STUDIES ON FUO

Study	Sharma (1992)[7]	Handa (1994)[33]	Dhawan (1994)[34]	Agarwal (1998)[35]
Infection	50%	48%	81%	61%

MATERIALS AND METHODS

Patients getting admitted to medical wards of Government Stanley Medical College and Hospital, Chennai, with fever and satisfying the below criteria were taken up for study. Patients of age group more than 12 years, both male and female were included.

INCLUSION CRITERIA

I. The following patients were included with number of days of fever less than 5 days and temperature >40°C or following organ dysfunction.

   a. With altered sensorium, seizures, signs of meningitis.

   b. Clinical signs suggestive of pneumonic consolidation.

   c. Signs suggestive of pleural effusion.

   d. Polyarthralgia

   e. Rash

   f. Purpura / ecchymoses

   g. Oliguria or serum creatinine > 1.5 mg/dl

   h. Jaundice or serum total bilirubin > 1.5 mg/dl

II. Fever of more than 5 days with or without organ dysfunction.

EXCLUSION CRITERIA

1. HIV seropositivity
2. Non - infectious causes of fever like hematological malignancy. connective tissue disorders and solid tumours were excluded from the study.

COMPARISON

Comparison of etiological profile with the previous study of 2002 - 2003.

THE FOLLOWING DATA WERE ANALYSED

PROFORMA

Name : Age : Sex : I.P. No :

Occupation and address :

1. SYMPTOMATOLOGY

FEVER

* Duration, pattern
* Rigors
* Other associated factors

RESPIRATORY SYSTEM

* Cough with expectoration
* Chest pain, hemoptysis
* Wheeze

CARDIOVASCULAR SYSTEM

* Chest pain, breathlessness
* Palpitations, syncope

ABDOMEN

* Nausea, vomiting, abdominal pain
* Loose stools, constipation
* Abdominal distension
* Jaundice

GENITOURINARY TRACT

* High coloured urine / hematuria
* Burning micturition
* Decreased urine output

NERVOUS SYSTEM

* Altered sensorium, head ache
* Seizures, motor weakness
* Cranial nerve symptoms
* Symptoms of in co-ordination

LOCOMOTOR SYSTEM

* Joint swelling / pain
* Muscle pain, back ache

SKIN / MUCOSA

* Rashes, purpuric spots, ecchymosis
* Vesications
* Oral mucosal lesions

EAR

* Ear ache / discharge

OTHERS

* Loss of appetite and weight
* Sore throat, neck swelling
* Leg swelling

PAST ILLNESS

* H/o. TB, DM, Rheumatic fever, Rheumatic heart disease, seizure disorder, sexually transmitted disease.
* H/o jaundice, blood transfusion
* H/o drugs, previous surgeries

PERSONAL HISTORY

* Smoking, alcohol, drug addiction
* Exposure (high risk behaviour)

FAMILY HISTORY

* H/o jaundice, tuberculosis

VITAL SIGNS

* Pulse
* Blood Pressure
* Temperature pattern
* Respiratory rate

2. GENERAL EXAMINATION

* Level of consciousness
* Temperature, hydration
* Clubbing, lymphadenopathy

* Rashes / petechiae / ecchymosis
* Pedal edema, arthritis
* Bony tenderness, spine tenderness

EXAMINATION OF

* Cardiovascular system
* Respiratory system
* Abdomen
* Nervous system

INVESTIGATIONS

* Blood : TC, DC, Hb%, PCV, ESR, Platelets
* Peripheral smear, cytology and parasites
* Blood urea, sugar
* Liver function test
* Blood culture and sensitivity
* ECG in all leads
* X-ray chest : PA view
* USG - abdomen
* Urine - albumin, sugar, deposits
* Urine - culture and sensitivity

If fever is >1 week

* Blood Widal
* Serology for Leptospirosis
* ELISA for HIV

In relevant cases, the following investigations were done :

* Sputum AFB, sputum culture and sensitivity, pleural fluid analysis
* Mantoux test
* Smear / QBC for malarial parasite
* CSF analysis
* Bone marrow study
* CT scan : Brain, chest, abdomen etc
* Lymph node : FNAC / Biopsy
* ANA, RF

DIAGNOSTIC CRITERIA

1. Tuberculosis

Patient was diagnosed to have pulmonary tuberculosis if any of the following criteria is satisfied.

* 2 initial sputum smear examination positive for AFB.
* Sputum smear examination positive for AFB and radiological abnormalities consistent with active pulmonary tuberculosis.
* Symptoms suggestive of TB with atleast 3 sputum examination negative for AFB and radiological abnormalities consistent with active pulmonary tuberculosis.

Extrampulmonary tuberculosis was diagnosed based on one culture positive specimen from the extrapulmonary site (or) histological evidence (or) strong clinical evidence consistent with active extrapulmonary TB.

2. Pneumonia was diagnosed based on clinical features, radiological findings, positive gram stain and sputum culture.

3. Meningitis was diagnosed based on clinical features, cytology, gram stain and culture of CSF, CSF - AFB and biochemistry.

4. Malaria was diagnosed based on clinical features, peripheral smear and quantitative buffy coat.

5. Leptospirosis was diagnosed based on clinical features, MSAT (macroscopic slide agglutination test) with a 2+ (or) 3+ positivity with modified Faine's score more than 25.

6. Enteric fever was diagnosed with WIDAL test, using a cut-off of $\geq$ 1/200 for O/H agglutinin titres, (or) a positive blood culture.

7. Rheumatic fever was diagnosed based on Modified Jones Criteria.

8. Infective endocarditis was diagnosed based on Duke's Criteria.

9. Liver abscess was diagnosed based on clinical features and ultrasonography.

10. Chikungunya fever was diagnosed by symptoms of fever with polyarthralgia during the epidemic.

11. Urinary tract infection was diagnosed based on symptoms and positive urine culture.

12. Other diseases were clinically diagnosed and confirmed by appropriate biochemical and radiological investigations.

RESULTS AND OBSERVATIONS

Total number of Cases	:	**500**
Diagnosed Cases	:	**429 (85.8%)**
Undiagnosed Cases	:	**71 (14.2%)**

The results of the study are analysed according to etiology, duration of fever, age and gender distribution.

TABLE - 1
ETIOLOGY OF FEVER

Sl.No.	Diseases	No.	Percentage
1.	Malaria	136	27.2%
2.	Leptospirosis	84	16.8%
3.	Tuberculosis	72	14.4%
4.	Pneumonia	41	8.2%
5.	Malaria & Leptospirosis	22	4.4%
6.	Chikungunya	18	3.8%
7.	Liver abscess	8	1.6%
8.	Urinary tract infection	8	1.6%
9.	Enteric fever	5	1%
10.	Rheumatic fever	5	1%
11.	Bacterial meningitis	3	0.6%
12.	Others	27	5.4%
13.	Undiagnosed	71	14.2%
	Total	**500**	**100%**

Malaria formed the largest group contributing to 27.2% of cases, followed by leptospirosis (16.8%), tuberculosis (14.4%) and pneumonia (8.2%).

TABLE - 2

GENDER WISE DISTRIBUTION

Sl.No.	Disease	Male	Female	Total
1.	Malaria	103	33	136
2.	Leptospirosis	41	43	84
3.	Tuberculosis	46	26	72
4.	Pneumonia	28	13	41
5.	Malaria & Leptospirosis	14	8	22
6.	Enteric fever	1	4	5
7.	Rheumatic fever	4	1	5
8.	Liver abscess	7	1	8
9.	Urinary tract infection	3	5	8
10.	Bacterial meningits	3	0	3
11.	Chikungunya	11	7	18
12.	Others	19	8	27
13.	Undiagnosed	44	27	71
	Total	**324 (64.8%)**	**176 (35.2%)**	**500 (100%)**

Males were more than females forming 64.8% of cases.

TABLE - 3

AGE WISE DISTRIBUTION IN FEVER CASES

Sl.No.	Disease	Age in Years			
		14-20	**21-40**	**41-60**	**>60**
1.	Malaria	41	55	29	11
2.	Leptospirosis	18	36	25	5
3.	Tuberculosis	9	32	25	6
4.	Pneumonia	3	13	18	7
5.	Malaria & Leptospirosis	4	12	5	1
6.	Chikungunya	3	12	3	-
7.	Liver abscess	1	6	-	1
8.	Urinary tract infection	2	4	2	-
9.	Enteric fever	1	2	1	1
10.	Rheumatic fever	5	-	-	-
11.	Bacterial meningitis	1	1	-	1
12.	Others	2	9	14	2
13.	Undiagnosed	16	27	14	14
	Total	**106 (21.2%)**	**209 (41.8%)**	**136 (27.2%)**	**49 (9.8%)**

Age group of 21 - 40 constituted the most common age group in our study forming about 42% of total cases studied.

TABLE - 4

FEVER DURATION AND DISEASE DISTRIBUTION

Sl. No.	Disease	<5 days	5-10 days	11-30 days	>30 days
1.	Malaria	51	57	24	4
2.	Leptospirosis	17	38	20	9
3.	Tuberculosis	1	21	25	25
4.	Pneumonia	13	19	4	5
5.	Malaria & Leptospirosis	8	10	1	3
6.	Chikungunya	12	4	2	-
7.	Liver Abscess	2	6	-	-
8.	Urinary tract infection	2	6	-	-
9.	Enteric fever	2	1	2	-
10.	Rheumatic fever	1	1	1	2
11.	Bacterial meningitis	2	1	-	-
12.	Others	6	10	6	5
13.	Undiagnosed	18	16	37	-
	Total	**135 (27%)**	**190 (38%)**	**122 (24.4%)**	**53 (10.6%)**

Most cases were admitted with fever durations of 5 - 10 days, forming 38% of cases.

MALARIA

- 37.5% had fever less than 5 days
- 75.7% were male
- 72.79% were within 40 yrs. of age
- Total cases : 136
  Plasmodium vivax : 120 cases
  Plasmodium falciparum : 15 cases
  Plasmodum vivax and Plasmodium falciparum : 1 case
  Survived : 129 cases
  Died : 7 cases

TABLE - 5

MALARIA - SYMPTOMATOLOGY

S. No.	Malaria	Total	PV	PF
1.	Chills & rigor	134 (98.5%)	118	15
2.	Head ache	74 (54.4%)	63	11
3.	Vomiting	48 (35.3%)	40	18
4.	Jaundice	4 (2.9%)	8	1
5.	Loss of consciousness	11 (8.0%)	11	0
6.	Seizures	6 (4.4%)	5	1
7.	Oliguria	6 (18.4%)	6	0
8.	Splenomegaly	25 (5.8%)	20	5
9.	Hepatosplenomegaly	8 (5.8%)	6	2

PV - Plasmodium vivax, PF - Plasmodium falciparum

Head ache and vomitting were most common symptoms along with fever.

TABLE - 6

JAUNDICE IN MALARIA

Sr. Bilirubin (mg/dl)	PV	PF	Total
1.5 - 3	7	3	10 (9.55%)
> 3	3	1	4 (2.4%)

Jaundice occurred in 26.66% of cases of falciparum and 8.33% cases of vivax.

TABLE - 7

RENAL FAILURE IN MALARIA

Sr. Creatinine (mg/dl)	P.V	PF	Total
1.5 - 3	10	1	(8%)
> 3	3	0	(2.20%)

No patients were dialysed

One patient died on conservative treatment

Renal failure occurred in 10.8% of cases of vivax and 6.6% cases of falciparum malaria.

TABLE - 8

CEREBRAL MALARIA

Manifestation	P.V	PF	Died
LOC	9	0	2
GTCS & LOC	2	0	0
GTCS	3	1	1

GTCS - Generalised tonic clonic seizures
LOC - Loss of consciousness

Cerebral malaria occurred in 11% cases of vivax 8.6% cases of falciparum.

Hypoglycemia occurred in 2 cases of vivax malaria

LEPTOSPIROSIS

- 16.8% of total cases studied
- Females constituted 51.2%
- 42.8% were in age group of 21 - 40 years
- 46% had fever of 5 - 10 days

TABLE - 9

LEPTOSPIROSIS - SYMPTOMATOLOGY

Symptom	Total	Male	Female
Myalgia	48 (57.14%)	24	24
Conj. Suffusion	28 (33.3%)	11	17
Jaundice	11 (13%)	11	0
Oliguria	4 (4.8%)	4	0

Myalgia and conjunctival suffusion were the most common symptoms along with fever.

TABLE - 10

LEPTOSPIROSIS - TOTAL BILIRUBIN

Sr. Bilirubin (mg/dl)	No. of cases
1.5 - 3	7 (8.33%)
> 3.0	9 (10.67%)
Total	**16 (19%)**

About one fifth of leptospirosis patients had icteric hepatitis.

TABLE - 11

LEPTOSPIROSIS - CREATININE

Sr.Creatinine (mg/dl)	No. of cases
1.5 - 3	8 (9.52%)
> 3.0	4 (4.48%)
Total	**12 (14%)**

About 14% of cases of leptospirosis had renal failure.

LEPTOSPIROSIS AND MALARIA CO-INFECTION

* Coinfection of leptospirosis and malaria formed 4.4% of cases included in the study.

* 63.6% were males and 36.4% were females.

* Plasmodium vivax was positive in 20 cases and Plasmdoium falciparum in 2 cases with confirmed leptospirosis in all cases.

* The organ dysfunction in co-infection are as follows :

TABLE - 12
MALARIA AND LEPTOSPIROSIS
- JAUNDICE

Sr.Bilirubin	No (%)
> 1.5	2 (9%)
> 3.0	7 (31.8%)
Total	**9 (39.8%)**

About two fifth of patients with malaria and leptospirosis coinfection had jaundice. All cases were positive for vivax malaria with leptospirosis.

TABLE - 13
MALARIA AND LEPTOSPIROSIS
- RENAL FAILURE

Sr.Creatinine mg/dl	No (%)
1.5 - 3	2 (9%)
> 3.0	NIL
Total	**2(9%)**

Both the cases had Plasmodium vivax malaria with leptospirosis.

TUBERCULOSIS

- 32% had fever more than 30 days
- 63.8% were males

TABLE - 14

ORGAN WISE DISTRIBUTION AMONG TUBERCULOSIS PATIENTS

Organ	M	F	Total %
Pulmonary	32	13	45(62.5%)
Pleural.effussion	9	7	16(22.22%)
Lymphadenitis	2	0	2(2.77%)
Meningitis	2	1	3(4.16%)
Pericardial effusion	-	1	1(1.38%)
Pyopneumothorax	0	1	1(1.38%)
Pneumothorax	0	1	1(1.38%)
Disseminated TB	1	1	2(2.77%)
	46	**36**	**72(100%)**

62.5% of the cases were pulmonary tuberculosis among total tuberculosis cases.

TABLE - 15

PULMONARY TUBERCULOSIS : SPUTUM STATUS

Sputum +ve for AFB	14 (31%)
Sputum -ve for AFB	31 (69%)

Sputum positivity was found in 31% of pulmonary tuberculosis patients.

TABLE - 16
PULMONARY TUBERCULOSIS - SYMPTOMATOLOGY

Symptom	Total	Percentage
Cough with sputum	40	88.88%
Breathlessness	33	73.33%
Loss of weight and loss of appetite	29	64.44%
Haemoptysis	12	26.66%

Sputum production was present in 88.88% of pulmonary tuberculosis patients.

TABLE - 17
SIGNS - CREPITATIONS

Lobe	No.	Percentage
Unilateral upper lobe	8	17.77%
Bilateral upper lobe	4	8.88%
Lower lobe	4	8.88%
Total	**16**	**35.52%**

Unilateral upper lobe crepitations were common.

TABLE - 18
REGION OF OPACITIES / CAVATIES IN CHEST - X-RAY IN PULMONARY TUBERCULOSIS

Site	No	Percentage
Bilateral apical opacity	5	11.11
Bilateral lower zone opacity	2	4.44
Right upper zone opacity	10	22.22
Left upper zone opacity	6	13.33
Right upper zone cavity	4	8.88
Right lower zone opacity	8	17.77
Left lower zone cavity	1	2.22
Left lower zone opacity	6	13.33
Bilateral extensive opacity	2	4.44
Bilateral cavity	1	2.22

Right upper zone opacity was the most common lesion constituting about 22.22%.

EXTRAPULMONARY TUBERCULOSIS

TUBERCULOUS PLEURAL EFFUSION

Total cases = 16

56.2% were males

56.2% were in age group 20 - 40 yrs.

TABLE - 19

SYMPTOMATOLOGY IN TUBERCULOUS PLEURAL EFFUSION

Symptoms	No. %
Cough with sputum	4 (25%)
Loss of weight and appetite	9 (56.6%)
Chest pain	7 (43.4%)

Loss of weight and appetite were the most common symptoms occurring in 56.6% of the cases.

TUBERCULOUS LYMPHADENITIS

2 Cases

- Both had cervical lymphadenopathy
- Both had low grade fever

TUBERCULOUS MENINGITIS

3 Cases

All the three had fever for 1 week

TABLE - 20

SYMPTOMS AND SIGNS IN TB MENINGITIS

Symptoms / Signs	No. (%)
Altered sensorium	1 (33.33%)
Loss of consciousness	1 (33.33%)
Meningeal Signs	3 (100%)

Meningeal signs were present in 100% of the cases.

TABLE - 21

DISSEMINATED TUBERCULOSIS : (2 CASES)

Features	Case - 1	Case - 2
Age	14	22
Sex	Male	Female
Lesion in Chest-X-ray	+	+
Pleural Effusion	+	+
Ascitis	-	+
Lymph node	-	+
Bone involvement	+	-
Joint involvement	+	-
Sputum	-ve	-ve

Widespread lesion were found where as sputum was negative in both cases.

PNEUMONIA

Total Cases - 41

65.88% were male

46.4% had fever for 5 - 10 days

43% were in age group 40 - 60 years

TABLE - 22

PNEUMONIA - SYMPTOMATOLOGY

S.No.	Symptom	No (%)
1.	Fever	41 (100%)
2.	Cough with sputum	41 (100%)
3.	Breathlessness	35 (85.36%)
4.	Chest pain	20 (48.7%)
5.	Haemoptysis	8 (19.5%)

Fever with cough and sputum were present in 100% of cases of pneumonia.

TABLE - 23

PNEUMONIA - BACTERIOLOGICAL PROFILE

Sl.No.	Organism	No. (%)
1.	K.pneumoniae	15 (53.57%)
2.	S.pneumonia	9 (32.14%)
3.	E.Coli	2 (7.14%)
4.	S.aureus	2 (7.14%)
	Total	**28 (100%)**

Klebsiella was the most common organism isolated constituting about 53.57% of isolates.

TABLE - 24

RADIOLOGICAL PROFILE IN PNEUMONIA CASES

Lung zone	Unilateral		Bilateral	Total
	Right	Left		
Upper zone	8	3	1	12(29.2%)
Lower zone	13	9	3	25(60.9%)
Mid zone	3	1	-	4(9.9%)
	24	13	4	41(100%)

Lower zone was the most common site of opacity in pneumonia constituting 61% of cases.

CHIKUNGUNYA

- Total Cases - 18
- Fever less than 5 days - 12 cases (67%)
- All had high grade fever
- 61.6% were male

TABLE - 25
CHIKUNGUNYA - SYMPTOMATOLOGY

Symptom	No (%)
Joint Pain	18 (100%)
Rash	4 (22.22%)
Pedal edema	6 (33.33%)
Puffiness of face	6 (33.33%)

Pedal oedema and puffiness of face was notable feature occurring in 33.33% of cases.

No organ dysfunction was noted in chikungunya cases.

TABLE - 26

CHIKUNGUNYA - JOINT INVOLVEMENT

Joint	No (%)
Knee Joint	14 (77.7%)
Ankle Joint	10 (55.5%)
Wrist Joint	12 (66.6%)
Small joints of hand	13 (72.2%)
Small joints of foot	8 (44.4%)

Knee joint was the most common joint involved.

Chikungunya IgM was positive in 2 cases.

LIVER ABSCESS

- Total Cases - 8
- Solitary abscess was present in 87.5% cases
- All of them had uncomplicated course
- 62.5% cases were managed conservatively and in 37.5% ultrasound guided aspiration of the fluid was done.

BACTERIAL MENINGITIS

- Total Cases - 3
- Males were 100%
- 66% had fever less than 5 days
- All had meningeal signs
- 1 patient had features of raised intracranial tension

URINARY TRACT INFECTION

- Total Cases - 8
- 62% were females
- 50% had E.coli and 50% had klebsiella grown in culture
- Most common group was 20 - 40 yrs.
- All of them responded to ciprofloxacin and cefotaxim.

RHEUMATIC FEVER

- Total Cases - 5
- 100% was of age less than 20 yrs.
- All of them had migratory polyarthiritis
- Most common cardiac lesion was mitral regurgitation (60% cases)

TABLE - 27
OTHERS - 27 CASES

Disease	No
Acute gastroenteritis	5
Suppurative lung disease	4
Sepsis	4
Cellulitis	4
Bronchiectasis	4
Filariasis	1
Empyema thoracis	1
Viral hepatitis	1
Post - varicella encephalitis	1
Acute cerebellitis	1
Post streptococcal glomerulonephritis	1

PROFILE IN UNDIAGONOSED CASES

- Total Cases - 71
- 61.9% were males
- 52% had fever more than 10 days but less than 30 days
- 38% were in the age group of 20 - 40 years.

TABLE - 28

ORGANOMEGALY IN UNDIAGNOSED FEVER CASES

Organ	No (%)
Splenomegaly	12 (16.9%)
Hepatomegaly	(5.6%)
Hepatosplenomegaly	4 (5.6%)
Total	**20 (28.1%)**

Organomegaly was noted in about 28% of undiagonosed fever cases.

ORGAN DYSFUNCTION IN FEVER CASES

TABLE - 29

JAUNDICE : 48 CASES

Sl.No.	Disease	Total Bilirubin		
		1.5-3 mg/dl	> 3mg/dl	Total
1.	Leptospirosis	7	9	16 (34%)
2.	Malaria	10	4	14 (29.7%)
3.	Malaria & Leptospirosis	2	7	9 (19.1%)
4.	Tuberculosis	2	0	2 (4.2%)
5.	Acute viral hepatitis	0	1	1 (2.1%)
6.	Undiagnosed	6	0	6 (12.76%)
	Total	27	21	48 (100%)

Leptospirosis was the most common cause of fever with jaundice constituting 34% of cases.

TABLE - 30
RENAL FAILURE - 52 CASES

	Disease	Sr.creatinine		
		1.5-3 mg/dl	**> 3.0mg/dl**	**Total**
1.	Malaria	11	3	14 (26.9%)
2.	Leptospirosis	8	4	12 (23%)
3.	Malaria & Leptospirosis	2	0	2 (3.7%)
4.	Pneumonia	4	0	4 (7.69%)
5.	Urinary tract infection	3	-	3 (5.76%)
6.	Cellulitis	1	1	2 (3.84%)
7.	Sepsis	1	2	3 (5.75%)
8.	Undiagnosed	11	1	12 (23.3%)
	Total	**41**	**11**	**52 (100%)**

Malaria was the most common cause of fever with renal failure comprising about 27% of cases.

TABLE - 31

NEUROLOGICAL DYSFUNCTION

Sl.No.	Disease (n = 30)	No (%)
1.	Cerebral malaria	16 (53.3%)
2.	T.B meningitis	3 (10%)
3.	Bacterial meningitis	3 (10%)
4.	Others	2 (6.66%)
6.	Undiagnosed	6 (20%)
	Total	**30 (100%)**

Cerebral malaria was the most common cause of neurological dysfunction with fever forming 53% of cases.

TABLE - 32

MORTALITY - TOTAL MORTALITY 21 CASES (4.2%)

Sl.No.	Disease	Male	Female	Total
1.	Malaria	3	4	7 (33.33%)
2.	Pneumonia	3	1	4 (19%)
3.	Sepsis	2	1	3 (14.28%)
4.	Leptospirosis	1	0	1 (4.76%)
5.	Tuberculosis	1	0	1 (4.76%)
6.	Others	5	0	5 (23.80%)
	Total	**15**	**6**	**21 (100%)**

Malaria was the most common cause of mortality constituting 33%.

TABLE - 33

MORTALITY IN MALARIA

Cause	Male	Female	Total
Cerebral malaria	1	2	3
ARDS	0	1	1
DIC	0	1	1
Sepsis	1	0	1
Sudden Death	1	0	1
Total	**3**	**4**	**7**

Among malaria, cerebral malaria was the commonest cause of mortality.

TABLE - 34

COMPARISON OF PRESENT STUDY WITH 2002 STUDY

Features	2002	2007
Total Cases	361	500
Diagnosed cases	195 (54%)	429 (85.8%)
Malaria	25 (12.8%)	136 (31.19%)
Leptospirosis	16 (8.2%)	84 (19.26%)
Tuberculosis	78(40%)	72 (16.51%)
Malaria & leptospirosis	(-)	22(5.04%)
Pneumonia	30(15.5%)	41(9.40%)
Undiagnosed	166 (46%)	71 (14.2%)

The number of diagnosed cases is 85.8% in present study white it was 54% in 2002 study. The percentages represent diagnosed cases.

DISCUSSION

500 patients, both male and female fulfilled the entry criteria and were included in the study. The patients were clinically examined and investigated following which 429 cases (85.8%) were diagnosed. The remaining 71 cases (14.2%) could not be diagnosed even after extensive investigations. However fever subsided in most undiagnosed cases after empiric antimalarial and antibiotic therapy.

Among the total cases malaria was the major contributor forming 27.2% of cases, followed by leptospirosis (16.8%) and tuberculosis (14.4%). Pneumonia formed 8.2%, co-infection with malaria and leprospirosis formed 4.4%, liver abscess - 1.6%, UTI - 1.6%, enteric fever - 1%, chikungunya - 3.8%, rheumatic reactivation - 1% and bacterial meningitis - 0.6% (Table - 1).

COMPARISION WITH OTHER STUDIES OF INFECTIOUS FEVERS

Similar study on clinical profile of infections fevers was carried out in Chennai in which there were more undiagnosed fevers[9].

The increased numbers of diagnosed cases in the present study (85.8%) in comparsion to previous study (54%) is probably due to increased diagnostic facilities (Table - 34).

Among the diagnosed cases number of malaria cases diagnosed in present study was 31.19% while it was 12.8% in the previous study. The increased incidence of malaria is due to use of peripheral smear and

quantitative buffy coat method which was carried out at malaria laboratory of Chennai Corporation.

Leptospirosis is diagnosed more often in the present study (19.26%) than the previous study (8.2%) due to awareness of the disease and picking up of anicteric leptospirosis and increased diagnostic facilities for doing slide agglutination test.

Chikungunya fever which was not present in the previous study was picked up in the present study due to the wide spread epidemic which occurred from July 2006 - December 2006.

The incidence of other causes of fever are more or less the same.

A similar study on etiological profile of fever was carried out in Thailand between 1999 - 2002, the results of which are similar to our study. Malaria constituted 25% of diagnosed cases in their study, whereas in our study it was 31%; leptospirosis was about 17%, in our study it constituted 19% of cases[10].

MALARIA

Malaria was the major contributor forming 27.2% of the total cases studied, which amounted to 136 cases. Plasmodium vivax occurred in 120(88%) cases, Plasmodium falciparum occurred in 15(11.2%) cases and mixed infection in 1(0.8%). Hazara et al.,[36] from calcutta has reported 73.3% PV and 26.7% PF in their study of 225 cases. Tamil Nadu is in low risk category with regard to Plasmodium falciparum infection.

CLINICAL FEATURES

In malaria 100% patients had fever. Typical paroxysms occurred in very few patients. Fever was associated in 95.5% cases with chills, in 54.4% head ache was severe and consistently associated with fever (Table - 5). **Mohapatra et al.,**[16] from Orissa reported migrainous head ache of 4.5% in a study of 110 cases of vivax malaria.

Along with clinical symptoms like vomitting, diarrhoea, myalgia and jaundice, pneumonia occurred in 5.14% cases.

CEREBRAL MALARIA

Cerebral malaria was a common complication noted in our study. 15 patients (11.02%) had neurological dysfunction in the form of altered sensorium, loss of consciousness and generalized convulsions. 9 patients (60%) had loss of consciousness. 4 (28%) had convulsions and 2 (12%) had both loss of consciousness and convulsions (Table - 8). Kochar[37] reported generalised convulsion in 21.31% of 441 cases of cerebral malaria from Rajasthan. 3 patients died of cerebral malaria all of which were caused by Pl.vivax. Cerebral malaria was associated with DIC in one case and one case was associated with jaumidce.

JAUNDICE

Jaundice occurred in 14 (10.29%) cases when the serum bilirubin cut off of more than 1.5 was taken. As per WHO criteria serum bilirubin of more than

3 mg% occurred in 4 cases (2.9%) (Table - 6). Bilirubinemia was predominantly direct, with only slight elevation of transaminases.

It occurred in 26.6% cases of falciparum malaria and 8.33% cases of vivax malaria. Hazara et al.,[36] reported jaundice in 9.09% of PV cases and 40% of PF cases. Harris VK et al., from South India reported 37% of jaundice in PF cases[38]. Kochar et al., from Rajasthan has reported jaundice in 58.85% of PF cases in 2001[18].

RENAL FAILURE

Acute renal failure occurred in 14 (10.29%) cases. As per WHO criteria severe renal failure occurred only in 2.20% of cases and all the cases were due to PV (Table - 7). In our study it has been found that renal failure also occurs in PV in significant numbers. This has been proved by kochar in his study of 11 cases of complicated vivax malaria by documenting the presence of PV and absence of PF by PCR study[19]. No patient was dialysed in our study. One patient died due to renal failure associated with ARDS. In India reported incidence of ARF in Malaria is 17.8% from Delhi, 17.2% from Orissa, 13% from North East India and 5.9% from Mumbai[39]. Madhu Muddaiah from Mangalore reported renal failure in 11.57% of 190 cases studied in 2002 - 2004[15].

OTHER COMPLICATIONS

Other complications noted were anaemia (Hb < 8 gm dl) which occured in 8% (11 cases). Hypoglycemia occurred in 2 cases. Both were due to PV malaria.

TREATMENT

Cases of plasmodium vivax malaria with organ dysfunction like jaundice, renal failure and cerebral malaria was treated with quinine and other cases were treated with chloroquine. Among the cases treated with chloroquine 17 (12.5%) showed chloroquine resistance while **Chowta et al.,**[17] noted chloroquine resistance in 16% of the cases.

MORTALITY

There were 7 deaths in malaria which accounted to 5.14% of total cases (Table - 32). Death due to cerebral malaria was 3 cases, and 1 case each of ARDS, DIC and sepsis expired.

LEPTOSPIROSIS

Leptospirosis contributed to 16.8% of total cases studied. Males constituted 48.8% and females 51.2%. Majority were in the age group of 21 - 40 years. Anicteric leptospirosis was about 81% while icteric leptospirosis formed 19% of cases. All of them were diagnosed using macroscopic slide agglutination > 2+ along with modified Faine's score of more than 25. Duration of fever was more than 5 days in 80% cases.

14.28% of our patients had renal failure while it was 79% **(Muthusethupathi et al.,)**[41] **and 49% (Edward et al.,)**[40] in other studies. The decreased renal failure in present study is probably due to decreased prevalence of serogroup autumnalis.

19% of patients had bilirubin of >1.5 mg/dl while it was 83% **(Muthusethupathi et al.,)[41] 95% (Edward et al.,)[40] and 28% (Gendron et al.,)[42]** in other studies.

Other unsual complication noted in the present study was pneumonia (10.71%) patients. Other complications were quadriparesis, hypovolemia, atrial fibrillation each occurred in 1.19% of cases.

63 patients recovered with doxycycline and 21 patients who had complication was treated with crystalline penicillin. One patient who had jaundice and renal failure expired.

CO-INFECTION OF MALARIA AND LEPTOSPIROSIS

A total of 22 (4.4%) patients had co-infection with both malaria and leptospirosis. Similar study on fever profile conducted in Thailand showed a co-infection of 5.5%[10]. An important observation was that 31.8% of co-infection patients had jaundice while renal failure was present only in 2 (9.04%) cases. It was present in 20 cases with PV and in 2 cases with PF.

TUBERCULOSIS

Tuberculosis was the third major contributor in our study constituting 14.4% of cases.

* 32% had fever more than 30 days

* 63.8% were males and 36.2% females

* Pulmonary tuberculosis contributed 62.5% cases with extrapulmonary TB forming 37.5% cases.

The contribution of tuberculosis was 54% **(Sharma et al.,)[7], 45% (Agarwal)[35] and 54% (Dhawan et al.,)[34]** in other studies.

PULMONARY TUBERCULOSIS

* Total - 45 cases

* Males constituted 71% and females 29%.

Among pulmonary tuberculosis, other symptoms along with fever was sputum which was present in 40 cases (88.88%). **Samal et al.,[27]** reported cough with expectoration in 92.7% of pulmonary tuberculosis cases. Haemoptysis was present in 25.5% while **Samal et al.,[27]** reported in 20.3% cases. Breathlessness was a complaint in 70.2% cases (Table - 16).

The most common radiological finding was unilateral upper zone opacity (34.04%), while **Samal et al.,[27]** most commonly reported bilateral scattered opacities in all zones in 77.5% cases.

Sputum AFB positivity was present in 30% of cases while **Dehankar et al.,[28]** reported sputum positivity in 42.34%. The expected ratio of recovery diagnosed smear positives : smear negatives under RNTCP is 50 : 50.

EXTRAPULMONARY TUBERCULOSIS

Tuberculous pleural effusion formed 22.22% of tuberculosis cases. Most (56.25%) were male. Fever duration was more than 15 days in 50% cases. Majority of them (56.25%) were in age group of 20 - 40 years. Next to fever chest pain was the most common symptom.

The other groups of extra pulmonary TB which constituted a minority was 2 cases of TB lymphadenopathy, 1 case of pyopneumothorax, 1 case of pneumothorax, and 1 case of tuberculous pericardial effusion.

In the case of tuberculous pericardial effusion pericardial fluid adenosine deaminase was measured which showed a value of 81 IU/L which is higher than the cut off value of 40 IU/L.

2 cases of disseminated TB was found out, both of them below 25 years age group and no specific immunosuppression was found out (Table - 21).

TB meningitis constituted about 4.16% (3 cases) of tuberculosis patients (Table - 20). All the 3 had duration of fever of 1 week. There was altered sensorium in 1, loss of consciousness in 1 case and meningeal signs were present in all the three and all cases were diagnosed by CSF studies.

Among the patients admitted 1(1.38%) case died, even with intensive management.

PNEUMONIA

Pneumonia formed significant number of cases in our study. It constituted about 8.2% (41 cases). Majority (65.85%) were male. Majority had fever of 5 - 10 days (46.3%).

Of the total cases, age group of 40 - 60 contributed to about 18 cases (43%). Etiological diagnosis was obtained in 68.2% while **Bansal et al.,** obtained etiological diagnosis in 75% of cases[29].

Patients older than 40 years were more predisposed as in the study by **Bansal et al**[29]. Cough with expectoration was present in 100% while **Narendra et al.,**[43] reported cough in 97.6%. In our study 85.36% had breathlessness 48.7% had chest pain (Table - 22). Most of the organisms isolated from the present study was sensitive to ciprofloxacin and gentamycin (Table - 23).

Important inference is that Klebsiella was the most common organism isolated in contrast to North American studies[44] in which S.pneumoniae was most common.

CHIKUNGUNYA

3.8% of cases in our study were due to Chikungunya fever. All of them had polyarthralgia with majority involving the knee joint (77%) and small joints of the hand (72%) (Table - 26). All the cases occurred during the Chikungunya epidemic of August - October 2006. Majority (66%) had fever less than 5 days duration. Pedal oedema and puffiness of face was present in 33% each. Other causes of polyarthragia was ruled out in these cases. All the

samples were sent to National institute of virology, Pune for analysis. In the cases fever subsided with antipyretics though there was prolonged joint pain.

LIVER ABSCESS

Liver abscess formed 1.6% of total cases. Most (75%) had fever of 5- 10 days, with males forming 87.5% of cases. 87.5% were in the age group of 20 - 40 years.

Abdominal pain (100%) was the most common symptom along with fever. Diagnosis was confirmed by ultrasonography.

62.35% cases was managed conservatively while 37.5% of cases were aspirated with ultrasonogram guidance.

URINARY TRACT INFECTION

UTI formed 1.6% of total cases. Diagnosis was based on symptomatology and urine culture. 62.5% were females. E.coli (62.5%) was the most common organism and none of them had complications.

RHEUMATIC FEVER

Rheumatic fever formed 1% of cases.80% were males and all were less than 20 years old. Ankle and knee joint was involved in the majority (60%) followed by wrist joint (40%). 80% had elevated ASO titre. 80% had mitral regurgitation by echo cardiogram.

All the patients were treated with aspirin 100 mg/kg and pain subsided within 2 days and subsequenly put on penicillin prophylaxis.

ENTERIC FEVER

Enteric fever was present in 1% of cases. 60% had fever more than 5 days. 80% were female. Along with fever headache, vomiting and diffise abdominal pain, splenomegaly was present in 40% of cases. Blood widal was positive in 100% of cases.

60% of patients responded to ciprofloxacin, while 40% of patients who did not respond to ciprofloxacin was treated with ceftriaxione. 3 had (32.5%) elevated creatinine at admission which recovered after treatment.

BACTERIAL MENINGITIS

Bacterial meningitis cases were 3 (0.6%) in our study. 2 (66%) had altered sensorium and none had seizures, while seizures was reported in 30% by **Pomeroy et al.,**[32] 100% had neck stiffness and Kernigs Sign. 1 had bilateral sixth nerve palsy. CSF examination showed predominant polymorphs and Gram stain was negative in all the three. All had low sugar and high protein and showed clinical improvement when cefotaxim 2 gm was used.

OTHER CAUSES

Suppurative lung disease, cellulitis, sepsis, acute gastroenteritis formed fewer number of cases (Table - 27). In most of the cases the diagnosis was clinical and supplemented by radiological and biochemical investigations.

Undiagnosed fever constituted 14.2% which were probably due to viral or partially treated malaria.

ORGAN DYSFUNCTION IN FEVER CASES

JAUNDICE

Of the total patients studied 48 patients (9.6%) had raised bilirubin of >1.5 mg %. Of these 44.68% (20 cases) had bilirubin >3 mg%. Of the total leptospirosis constituted 34% of cases (16), while co-infection constituted 19.14% and malaria 29.78% of cases (Table - 29). Acute viral hepatits was the cause in 1 case. Hepatitis B was positive in this case. The cause of fever with jaundice was not diagnosable in 12.76% of the cases.

RENAL FAILURE

Renal failure with creatinine >1.5 mg/dl was present in 10.4% (52 cases), of which severe renal failure with creatinine >3 mg/dl was present in 19.23% of total renal failure cases. Of the total renal failure cases 26.9% was constituted by malaria and 23% was constituted by leptospirosis (Table - 30). Pneumonia constituted 7.69% cases of renal failure. The cause of fever with renal failure was undiagonosed in 12 (25% of cases), probably due to partialy treated malaria and leptospirosis which would have rendered these test negative.

NEUROLOGICAL DYSFUNCTION

Neurological dysfunction was present in 6% (30 cases), most constituted by malaria (53.3%) (Table - 31). TB meningitis and bacterial meningitis

constituted 3% each. Acute cerebellitis and post varicella encephalitis constituted 3.33% each. 20% (6 cases) were undiagonosed, are probably due to smear negative cerebral malaria or partially treated meningitis referred from outside.

MORTALITY

The overall mortality is 4.2% the most common cause is malaria constituting 33.3% of all deaths. The various profile in malaria death were cerebral malaria - 3 ARDS - 1, DIC - 1, sepsis - 1, sudden death - 1 (Table - 32).

Pneumonia formed 19.04% (4) of total deaths. 50% were more than 50 years.

SUMMARY

1. 500 patients were analysed, 64.8% were males and 35.2% were females.

2. Etiology of febrile illness could be diagnosed in 85.8% cases.

3. The common causes of infectious fever were malaria (27.2%), leptospirosis (16.8%) tuberculosis (14.4%) and pneumonia (8.2%). Other causes were chikungunya (3.8%), urinary tract infection (1.6%) liver abscess (1.6%), rheumatic fever (1%) and enteric fever (1%).

4. Plasmodium vivax formed 88% of malaria cases while plasmodium falciparum occured in 12%.

5. Common complications of malaria were Cerebral malaria (11.02%), jaundice (10.29%) and renal failure (10.29%).

6. Anicteric leptospirosis (81%) was the most common presentation and renal failure occurred in 14% of the cases.

7. The most common presentation of tuberculosis was pulmonary tuberculosis (62.5%). Extrapulmonary tuberculosis occured in 37.5%

8. Klebsiella was the most common organism isolated in cases of pneumonia (53.7%) followed by pneumococci and Staphylococcus aureus.

9. Co-infection with malaria and leptospirosis occurred in 22 (4.4%) patients. Among the cases of malaria, co-infection with leptospirosis occurred in 14% cases.

10. Chikungunya fever occurred in 18(3.8%) patients.

11. Rheumatic fever and enteric fever occurred in 5(1%) cases each.

12. Bronchiectasis, suppurative lung diseases and sepsis occurred in less than 1% cases..

13. Jaundice with fever occurred in 48(9.6%) patients. Leptospirosis contributed to 34% and malaria to 30%.

14. Fever with renal failure occurred in 52(10.4%) patients. Malaria contributed to 30% and leprospirosis to 23%.

15. Malaria was the most common cause of neurological dysfunction contributing to 53% of cases.

16. Mortality was 21(4.2%) cases in the study, malaria contributing to 7 cases and pneumonia to 4 cases.

17. Comparing this study with the previous study carried out in Chennai in 2002 - 2003, there is increase in incidence of malaria and leptospirosis with lesser number cases of tuberculosis, probably due to increased diagnostic facilities. There is also a increase in percentage of diagnosed cases from 54% in 2002 to 86% in the present study.

CONCLUSION

500 admitted febrile patients were evaluated. Etiology of febrile illnesses could be diagnosed in 86% of the cases. This was much higher than the previous study (54%). This is probably due to the availability of better diagnostic facilities. Malaria, leptospirosis, tuberculosis and pneumonia were the common causes of infectious fevers in this study. Availability of simple diagnostic facilities will improve the reporting of these illness and thereby reducing the mortality associated with infectious diseases.

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